

Preliminary communication

## They know their trauma by heart: An assessment of psychophysiological failure to recover in PTSD



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### ABSTRACT

**Background:** Posttraumatic stress disorder (PTSD) develops following exposure to a traumatic event and is characterized by persistent intense reactivity to trauma related cues. Equally important, but less studied, is the failure to restore physiological homeostasis after these excessive reactions. This study investigates psychophysiological markers of sustained cardiac activity after exposure to reminders of traumatic event in PTSD patients.

**Methods:** Participants passively listened to neutral and personal traumatic event while electrocardiogram was continuously recorded. Heart rate (HR) and heart rate variability (HRV) were analyzed in 19 PTSD patients and 16 trauma-exposed controls.

**Results:** Both PTSD patients and trauma exposed controls exhibited a significant increase in HR to the exposure of their personal trauma. PTSD patients sustained the increase of HR while controls recovered to basal levels. In PTSD patients, sustained HR was positively associated with re-experiencing symptoms. The PTSD group also showed a reduced HRV (a measure of parasympathetic influence on the heart) during personal trauma exposure and lack of recovery.

**Limitations:** The sample size was small and PTSD patients were under medication.

**Conclusions:** Our findings provide an experimental account of the failure of PTSD patients to exhibit physiological recovery after exposure to trauma-related stimuli. PTSD patients exhibited a sustained tachycardia with attenuation of HRV that persisted even after cessation of the stressor. Re-experiencing symptoms facilitated engagement in the trauma cues, suggesting that, in their daily-life, patients most likely present repeated episodes of sustained over-reactivity, which may underpin the emotional dysregulation characteristic of PTSD.

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## 1. Introduction

The diagnostic criteria for posttraumatic stress disorder (PTSD) require experiencing, witnessing, or being confronted with “an event or events that involved actual or threatened death or serious injury, or a threat to the physical integrity of self or others” (American Psychiatric Association, 1994). Diagnostic criteria also require that the individual experience intense fear, helplessness, or horror during the traumatic event. According to the DSM-IV, the definition of PTSD also includes three symptoms clusters: re-experiencing, avoidance and numbing, and

hyperarousal. These symptoms must continue for more than 1 month and must cause significant distress and impairment. PTSD is a chronic illness, and it leads to significant public health consequences; including increased rates of unemployment, marital instability and suicide (Kessler, 2000); impaired role functioning and health problems (Zayfert et al., 2002); cognitive impairments (Mueller-Pfeiffer et al., 2010); and secondary mental disorders, such as substance dependence (Breslau, 2002; Breslau et al., 2003).

PTSD pathology includes an excessive reaction to internal or external cues that resemble the traumatic event. Researchers have provided many relevant pathophysiological insights into PTSD symptomatology using laboratory assessments, which typically employ non-invasive biological recordings related to trauma memories. Autonomic hyperarousal during trauma-related cues has been demonstrated in many different experimental paradigms, including

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hearing aversive unexpected sounds (Holstein et al., 2010), viewing pictures (Rabe et al., 2006), videos (Hauschildt et al., 2011) or words (Bremner et al., 2003) related to the trauma, or when the subject recounts and/or listens the traumatic event (Cohen et al., 1998; McTeague et al., 2010).

A meta-analysis of the psychophysiology of PTSD (Pole, 2007) showed that patients exhibit an elevated reactivity to external and internal trauma reminders. This striking excess in arousal and reactivity has led most investigators to emphasize biological systems involved in reacting to trauma-related cues. However, PTSD can also be conceptualized as a disorder related to failure of recovery mechanisms impeding the restitution of physiological homeostasis (Yehuda and LeDoux, 2007). Indeed, the meta-analysis by Pole (2007) highlighted that, rather than the reactivity to trauma-related cues, the most robust effect to note in PTSD was the failure to show recovery.

The personal trauma script-driven imagery protocol is widely used to elicit PTSD symptoms. In this paradigm, the participant listens to an autobiographical script and is instructed to mentally relive the event as vividly as possible during and after audio playback (Lang et al., 1980; Pitman et al., 1987). Physiological reactivity during personal threat imagery is significant in PTSD patients as well as in controls (McTeague et al., 2010). A previous study (Volchan et al., 2011) employed passive listening to personal trauma script (without imagery instructions), an experimental condition with more resemblance to real contexts. Volchan et al. (2011) showed that even without imagery instructions the trauma cue triggered a last-ditch defense response (tonic immobility) following the end of audio play in a larger proportion of PTSD patients than in trauma-exposed controls. The authors raised the possibility that re-experiencing symptoms was responsible for the different and sustained engagement of patients, relative to controls, following exposure to trauma cues without imagery instructions.

The aim of the present study is to investigate the psychophysiological markers of sustained cardiac activity after exposure to reminders of the traumatic event in PTSD patients. For this purpose, we contrasted the cardiac activity of trauma-exposed victims with and without PTSD, both during and after presentation of their personalized trauma script without imagery instructions. We hypothesized that PTSD patients would show more cardiac reactivity than controls during exposure to their trauma script and, most importantly, we hypothesized that patients would sustain this high reactivity after exposure, while controls would recover. Furthermore, we speculated that re-experiencing symptoms would be critical for the sustained reactivity in PTSD patients.

## 2. Methods

### 2.1. Participants

Nineteen patients with primary diagnoses of PTSD (10 men, 9 women) aged 22–53 years ( $M=39.8$ ,  $SD=7.53$ ) were recruited from an outpatient University clinic specialized in posttraumatic stress assessment and treatment. Psychiatric diagnoses were obtained using the Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) Axis I (First et al., 1997), translated and adapted into Portuguese by Del-Ben et al. (2001). Exclusion criteria were psychotic disorders, severe personality disorders, and significant cognitive impairment. Major depression was the most frequent comorbidity (84.2%).

Sixteen trauma-exposed controls (9 men, 7 women) aged 26–55 years ( $M=41.7$ ,  $SD=8.75$ ) without PTSD were also recruited. This group met criteria A1 and A2 of DSM-IV.

Posttraumatic stress symptoms were assessed in both groups using the Posttraumatic Stress Disorder Checklist–Civilian Version (PCL-C) (Weathers et al., 1993), translated and adapted to Portuguese by Berger et al. (2004). The PCL-C is a 17-item self-report measure of the severity of symptoms in response to a traumatic experience. Using a 5-point Likert scale (1 = not at all, 5 = extremely), participants rated the extent to which each symptom has disturbed them in the past month, providing a total symptom score and a score for each cluster (re-experiencing, avoidance and numbing, and hyperarousal). For the trauma-exposed control group, inclusion criterion required scores < 35 on the PCL-C, which is one of the most conservative cutoffs for PTSD screening (McDonald and Calhoun, 2010).

The predominant index trauma for both PTSD patients and trauma-exposed controls was urban violence. PTSD patients were under pharmacological treatment with antidepressant drugs in adequate doses according to the recommended guidelines for PTSD (Friedman et al., 2008). Other data from some participants in this sample were described in a previous study (Volchan et al., 2011).

### 2.2. Autobiographical scripts

The protocol for personal traumatic scripts was based on previous studies (Lang et al., 1980; Lang, 1979; Pitman et al., 1987). Participants meticulously narrated their most traumatic event and described their physical reactions during the event. Details collected about traumatic events included the following: date, time, location, sensory stimuli, defense reactions, emotional reactions, and the presence of others. We summarized personal traumatic scripts so that they consisted of the most terrifying moment reported by the participants. The scripts comprised exactly 100 words, each chronologically portraying the traumatic experience in the second person and the present tense. We also created neutral scripts composed of exactly 100 words that depicted shopping in a grocery store. Each neutral script was partially personalized in that we matched the number of people and the action verbs involved in the personal traumatic history. A male professional speaker recorded the 60-s scripts in a neutral voice for later playback and presentation to the participants.

### 2.3. Physiological measures

The scripts were presented and electrocardiogram data were acquired on two PCs running Presentation (Neurobehavioral Systems) and Acknowledge (BIOPAC Systems Inc.) software, respectively.

Electrocardiogram recordings were collected at a sampling frequency of 1000 Hz through an ECG100C module coupled to the MP150 system (BIOPAC Systems Inc.). An off-line peak detection algorithm (derivative plus threshold) was used to estimate R wave fiducial points, after which the series was screened by hand and corrected for artifacts. Heart rate was derived from the interval (in ms) between successive R waves and was later converted to beats per minute. A time-domain measure of heart rate variability was calculated as the root mean square of successive differences between adjacent R–R intervals (RMSSD).

Data processing followed the recommendations of the Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology (1996). We employed KARDIA, a Matlab (MathWorks Inc., MA) software, for the analysis of cardiac parameters (Perakakis et al., 2010).

### 2.4. Procedure

The local Institutional Ethics Review Board approved this study, and participants provided informed consent before assessment.

The participants were informed that they could withdraw from the experiment at any time.

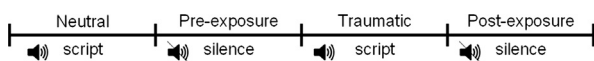
The experiment sessions occurred in a light- and sound-attenuated room. The participants were seated and had electrocardiogram electrodes attached to their chest. Basal recordings were collected for 10 min. Scripts were played while participants remained in a standing position. The stimulus presentation followed a standard sequence: instructions (20 s), silent interval (60 s), neutral script (60 s), pre-exposure (60 s), traumatic script (60 s), and post-exposure (60 s) (Fig. 1). The scripts were presented without any explicit instructions to “pay attention” or to “vividly try to re-experience” the situation; the participants were simply instructed to passively listen to the scripts.

### 2.5. Statistical analysis

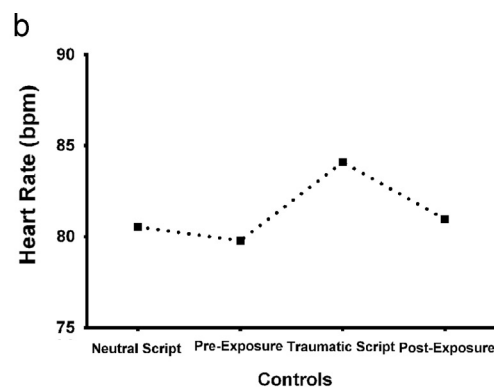
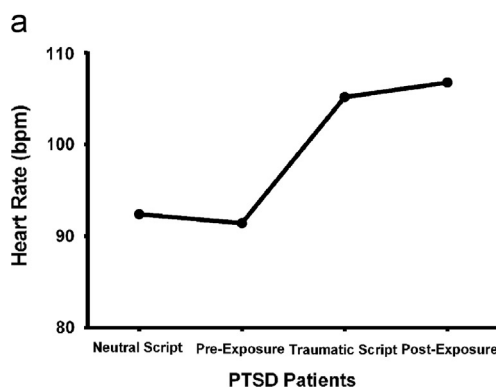
Data were analyzed using Statistica 7.0 (StatSoft, Inc.). Because the data did not follow a Gaussian distribution, only non-parametric tests were used.

Basal heart rate and heart rate variability were calculated for the last 5 min of the basal period, and comparisons between PTSD patients and trauma-exposed controls were performed using Mann–Whitney tests. Two patients were excluded from the analysis of basal heart rate variability due to sporadic arrhythmias.

The modulation of heart rate along the conditions was calculated for the 60-s duration of each condition (neutral script, pre-exposure, traumatic script and post-exposure). The modulation of heart rate variability along the conditions was calculated for a lesser duration (40 s) to include data from the two patients with sporadic arrhythmias. We used Friedman variance analyses for repeated measures, separately for PTSD patients and trauma-exposed controls. Where we found statistically significant results, we additionally used Wilcoxon signed rank post hoc tests to compare conditions of interest. To investigate cardiac activity, we compared corresponding conditions, that is, conditions with playback (traumatic script vs. neutral script) in one analysis and conditions without playback (pre-exposure vs. post-exposure) in another analysis. The former would represent cardiac reactivity to script audio play, whereas the latter would represent sustained cardiac reactivity after script audio play. Additionally, failure to recover was investigated by comparing cardiac parameters collected during playback of traumatic script with that during the post-exposure period.



**Fig. 1.** Sequential conditions of the experimental session. Neutral script: audio-play of a neutral history; pre-exposure silence: interval without audio-play; traumatic script: audio-play of personal trauma; and post-exposure silence: interval without audio-play.



**Fig. 2.** Mean heart rate during each experimental condition for PTSD patients (a) and trauma-exposed controls (b). bpm, beats per minute.

We also investigated if failure to recover was correlated with PTSD cluster symptoms. One index of sustained cardiac reactivity consisted of the difference in heart parameters (heart rate, heart rate variability) between the period of post-exposure minus the period of pre-exposure divided by the period of pre-exposure (index 1). The other index of sustained cardiac reactivity consisted of the difference in heart parameters between the post-exposure period minus the traumatic script period (index 2). Spearman correlation tests were used to determine whether each cluster of posttraumatic symptoms correlated with either of the cardiac indexes.

In all analyses, we considered  $p$  values  $< 0.05$  as statistically significant.

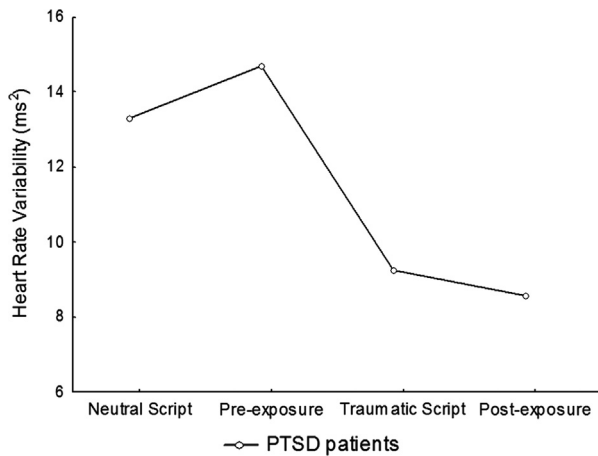
### 3. Results

Basal heart rate was significantly higher for PTSD patients than for trauma-exposed controls ( $z=2.31$ ,  $U=69.0$ ,  $p=0.02$ ). Basal heart rate variability was significantly lower for PTSD patients than for trauma-exposed controls ( $z=-2.23$ ,  $U=74.0$ ,  $p=0.02$ ).

Analysis of the modulation of heart rate along the conditions (neutral script, pre-exposure, traumatic script and post-exposure) in PTSD patients revealed a significant main effect ( $\chi^2=31.86$ ,  $p=0.0001$ ) (Fig. 2a). Post hoc Wilcoxon signed rank tests showed an increase in heart rate during exposure to the traumatic script in comparison with the neutral script ( $z=3.70$ ,  $p=0.0002$ ). There was also an increase in heart rate during the post-exposure period compared with the pre-exposure period ( $z=3.42$ ,  $p=0.0006$ ); Finally, PTSD patients demonstrated no significant change in heart rate between the exposure to traumatic script and the post-exposure period ( $z=0.20$ ,  $p=0.84$ ), suggesting that they sustained an accelerated heart rate even after cessation of the stressor stimulus.

The modulation of heart rate along the conditions in trauma-exposed controls also showed a significant main effect ( $\chi^2=14.02$ ,  $p=0.002$ ) (Fig. 2b). Post hoc tests showed an increase in heart rate during exposure to the traumatic script in comparison with the neutral script ( $z=2.27$ ,  $p=0.02$ ). Comparison between the post-exposure period and the pre-exposure period was not significant ( $z=0.20$ ,  $p=0.8$ ). Importantly, the control group showed a significantly reduced heart rate during post-exposure relative to during traumatic script exposure ( $z=2.63$ ,  $p=0.008$ ).

Analysis of heart rate variability along the conditions in PTSD patients showed a significant main effect ( $\chi^2=14.31$ ,  $p=0.01$ ) (Fig. 3). Post hoc tests showed a reduction in heart rate variability during the exposure to traumatic script in comparison with the neutral script ( $z=2.69$ ,  $p=0.007$ ), and a reduction in heart rate variability during post-exposure period in comparison with pre-exposure period ( $z=2.81$ ,  $p=0.004$ ). Similarly to heart rate analysis, PTSD patients



**Fig. 3.** Mean heart rate variability during each experimental condition for PTSD patients.

**Table 1**  
Correlations between sustained heart rate indexes and posttraumatic symptomatology.

PTSD symptoms	Spearman $\rho$	<i>p</i> value
<b>Index 1</b>		
PCL-C Total	0.40	0.09
Re-experiencing	0.49	0.03
Avoidance/numbing	0.30	0.22
Hyperarousal	0.21	0.39
<b>Index 2</b>		
PCL-C Total	0.51	0.02
Re-experiencing	0.54	0.01
Avoidance/numbing	0.42	0.08
Hyperarousal	0.43	0.08

Index 1, post-exposure minus pre-exposure, divided by pre-exposure; Index 2, post-exposure minus traumatic script; PCL-C, Posttraumatic Stress Disorder Checklist-Civilian Version

showed no significant change in heart rate variability between the post-exposure period and the exposure to traumatic script ( $z=0.89$ ,  $p=0.8$ ), suggesting that the decrease in heart rate variability was sustained even after cessation of the stressor.

In trauma-exposed controls, no significant modulation of heart rate variability along the conditions was found ( $\chi^2=2.28$ ,  $p=0.48$ ).

Investigation of the relationship between cardiac indexes and PTSD cluster symptoms were conducted only in PTSD patients, and Table 1 summarizes the results.

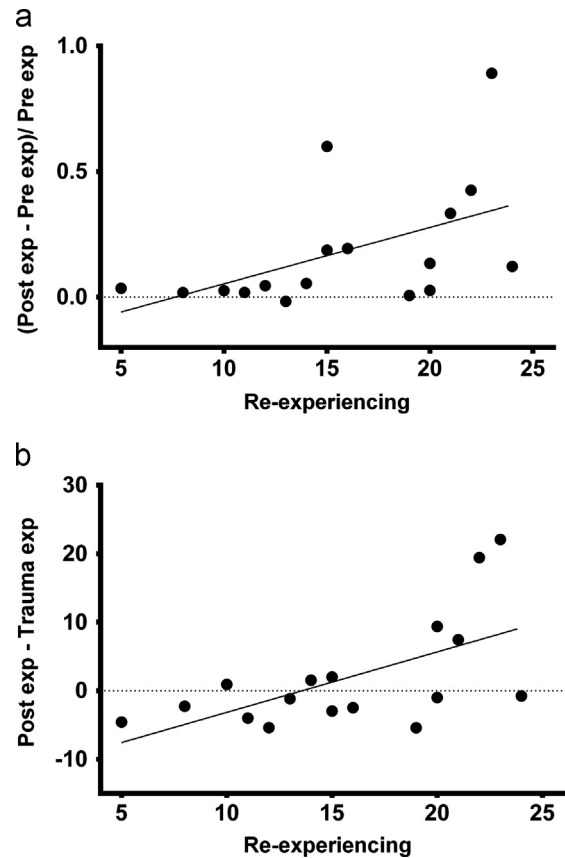
For heart rate, there was a significant correlation ( $\rho=0.49$ ,  $p=0.03$ ) between re-experiencing scores and index 1 (which contrasts heart rate post- with pre-exposure) indicating that patients with more re-experiencing symptoms showed the highest enhance in heart rate (Fig. 4a). There was also a significant correlation ( $\rho=0.54$ ,  $p=0.01$ ) between re-experiencing scores and index 2 (which contrasts heart rate post-exposure with that during exposure) (Fig. 4b). The latter shows that tachycardia can rise beyond exposure levels in patients with high levels of re-experiencing symptoms.

There was a significant correlation ( $\rho=0.51$ ;  $p=0.02$ ) between total symptoms' scores and index 2. No other significant correlations for heart rate indexes and PTSD symptoms were found.

No significant correlations were found between heart rate variability indexes and PTSD symptoms.

**4. Discussion**

This study investigated failure of cardiac recovery following passive listening to an audiotaped personal trauma script and the



**Fig. 4.** Correlations between indexes of heart rate sustained reactivity and re-experiencing symptoms. (a) Index 1. Post-exposure minus pre-exposure, divided by pre-exposure (post exp – pre exp)/pre exp; and (b): Index 2. Post-exposure minus trauma exposure (post exp – trauma exp).

influence of the cluster of re-experiencing symptoms on sustained reactivity in PTSD patients.

**4.1. Resting cardiac activity**

PTSD patients showed a higher basal heart rate than trauma-exposed controls. This result is in line with other physiological studies of PTSD (Buckley and Kaloupek, 2001; Orr and Roth, 2000; Pole, 2007). It is interesting to note that a high basal heart rate in the aftermath of trauma was shown to be a significant predictor of the development of this disorder (Bryant et al., 2011).

Basal heart rate variability in PTSD patients was significantly lower than in trauma-exposed controls. This result is congruent with others studies that found lower basal heart rate variability in trauma-exposed participants with PTSD compared to those without PTSD (Cohen et al., 1997, 1998, 2000a, 2000b; Blechert et al., 2007; Hughes et al., 2006, 2007a, 2007b; Mitani et al., 2006; Tan et al., 2009).

**4.2. Failure to recover: sustained cardiac reactivity in PTSD**

The current findings demonstrate that both PTSD patients and trauma-exposed controls exhibit a significant heart rate reaction upon exposure to a traumatic script but that only PTSD patients present sustained cardiac reactivity following traumatic script presentation.

Previous script-driven protocols to evoke physiological reactivity in PTSD were based upon imagery instructions. These instructions required participants to vividly relive their trauma both during listening and during a post-exposure period (Lang et al.,



1980; Pitman et al., 1987). Studies of cardiac reactions in anxiety disorders that have employed this protocol have observed a significant acceleration in heart rate during script presentation and an even higher heart rate in the post-exposure period (e.g., Lang et al., 1998; Pitman et al., 1987). Furthermore, script-driven imagery studies in PTSD have found that both patients and controls show a significant reaction during imagery (albeit this reaction is less robust in controls) (McTeague et al., 2010), revealing that imagery instructions are potent evokers of cardiac reactions even in the absence of psychopathology. In our study, in spite of not receiving any imagery instructions, PTSD patients still showed a robust increase in heart rate during traumatic script presentation and a sustained tachycardia in post-exposure (when no external stimuli were administered). However, trauma-exposed controls presented a significant (although feebler) heart rate response to traumatic script but recovered to basal levels when traumatic script presentation ended. Thus, compared to trauma-exposed controls, PTSD patients showed both an over-reaction during passive listening to their traumatic script and a subsequent failure to recover. It has been shown (see Jovanovic et al., 2012 for a review) that PTSD patients have impaired safety signal processing expressed as a difficulty in responding to safety cues physiologically, even when cognitively aware of it. Although they are safe in the laboratory setting, the present results showed that most PTSD patients respond to reminders of the trauma similarly to the real danger situation.

In the present study, heart rate variability in PTSD patients decreased significantly during traumatic script presentation and remained reduced thereafter. This reduction suggests a sustained decrease in parasympathetic outflow to the heart. Trauma-exposed controls did not show significant changes in heart rate variability at any point in the experimental session.

Taken together, the modulation of both cardiac parameters reported here seems to point to a deficient vagal control of the heart in PTSD patients.

#### 4.3. Re-experiencing symptoms and over-engagement in external cues in PTSD

PTSD patients with more re-experiencing symptoms showed significantly higher heart rates following traumatic script exposure (see Fig. 4b). These results indicate that patients presenting more re-experiencing symptoms engaged more deeply in the script induction, as they showed robust heart rate acceleration to the traumatic script that was sustained or potentiated after exposure.

According to Pitman (1989), high adrenergic activity during a traumatic event could over-consolidate memories. These memories may become so deeply ingrained in the traumatized individual's mind that memory extinction is inhibited and memories continually re-surface through re-experiencing symptoms. DSM-IV criteria for the re-experiencing cluster comprise spontaneous unwanted memories of the traumatic event. These include intrusive recollections, nightmares and flashbacks as well as physical symptoms triggered by external cues. These criteria may be in line with our findings that among other symptoms only the re-experiencing cluster was significantly correlated with heart rate changes from pre-exposure to post-exposure, and with heart rate changes from trauma exposure to post-exposure.

#### 4.4. Potential clinical implications

Our data suggest that the effects of a traumatic cue do not end with the removal of that stressor. Exposure to a personal traumatic script without imagery instructions can trigger significant and sustained cardiac reactivity in PTSD patients.

Repeated events of strong and sustained tachycardia, accompanied by sustained reduced heart rate variability (a measure of parasympathetic influence on the heart), may underpin the numerous findings of increased risk of cardiovascular disease in PTSD (Dedert et al., 2010). Several studies have shown that low heart rate variability is a strong predictor of cardiovascular morbidity and mortality (Thayer and Lane, 2007). Our study has significant clinical implications for the early detection and prevention of cardiovascular disease, and it suggests that integrated physical and mental health treatments could benefit long-term trajectories in PTSD.

Indeed, different PTSD treatments have in common the enhancement of heart rate variability in association with a reduction in PTSD severity. The studies include diverse treatments such as heart rate variability biofeedback (Zucker et al., 2009; Tan et al., 2011), eye movement desensitization and reprocessing (EMDR; Sack et al., 2008), fluoxetine treatment (Cohen et al., 2000b), and cognitive behavioral therapy (CBT; Nishith et al., 2003; Norte et al., 2011; Hinton et al., 2009).

Strong re-experiencing symptoms seems to prone PTSD patients to more deeply engage in traumatic script and trigger cardiac acceleration even in an experimental paradigm, which, as in our study, does not employ explicit instructions to relieve the trauma. Moreover, given the present findings, it seems likely that patients repeatedly engage in strong and sustained stress reactivity in their daily life. Psychotherapeutic interventions that focus directly on the management of re-experiencing symptoms should be emphasized in clinical settings, as they capture the emotional dysregulation characteristic of PTSD and its hyper-responsive expression.

#### 4.5. Limitations

There are some limitations to the present study. First, our study is limited by its small sample size. Second, our PTSD patients were taking psychiatric medications and were known to have comorbid psychiatric illnesses.

## 5. Conclusions

The present work investigated cardiac activity in PTSD patients following passive exposure to their traumatic experience. This procedure is more closely related to potential real-life triggers than those more widely used in the psychophysiological assessment of PTSD. Here, there were no instrumental instructions or cognitive/imagery tasks to be accomplished by the participant.

Our findings provided an experimental account for the failure of PTSD patients to exhibit physiological recovery after exposure to trauma-related stimuli. This failure to recover is associated with re-experiencing symptoms and with deficient vagal control. Replications of the current findings as well as the delineation of more qualitative and quantitative measures may help to clarify the emotional dysregulation characteristic of PTSD and its physiological expression.

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### Conflict of interest

The other authors have no conflict of interest to disclose regarding this research.

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